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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,817	03/07/2006	Russell Mumper	050229-0447	8574

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,817	MUMPER ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 1987*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7, 9, and 11-26* is/are pending in the application.

4a) Of the above claim(s) *9 and 15-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 11-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

An amendment was received and entered on 1/15/08.

Claims 8 and 10 were canceled.

Claims 9 and 15-26 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/9/07.

Claims 1-7, 9, and 11-26 are pending in the application.

Claims 1-7 and 11-14 are under consideration.

Rejections and objections not reiterated here are withdrawn.

Priority

The instant application is the national stage of PCT/US03/29536, filed 9/24/03 which claims benefit of US Provisional Application 60/412,780, filed 9/24/02. The provisional application fails to provide support for nanoparticles that are not cationic, such as those embraced by instant claims 1, 3-7, and 11-14. Accordingly the effective filing date of claims 1, 3-7, and 11-14. The effective filing date of claim 2 is 9/24/02.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 11, 13, and 14 stand rejected under 35 U.S.C. 102(b) and (e) as being anticipated by Langer et al (US 20020131951, published 3/19/02).

Langer taught compositions comprising an adjuvant such as cholera toxin and cationic nanoparticles comprising a nucleic acid encoding a polypeptide antigen. See abstract and paragraphs 37, 90, 91, and 99 on pages 4, 11 and 12. The nucleic acid can be DNA or an oligonucleotide, see paragraphs 11 and 39 on pages 2 and 4. Absent a limiting definition in the instant specification, the term "oligonucleotide" is considered to embrace the antigen encoding nucleic acids of Langer.

Claim 2 stands rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Langer et al (US 20020131951).

Langer taught compositions comprising an adjuvant such as cholera toxin and cationic nanoparticles comprising a nucleic acid encoding a polypeptide antigen. See abstract and paragraphs 37, 90, 91, and 99 on pages 4, 11 and 12. The nucleic acid can be DNA or an oligonucleotide, see paragraphs 11 and 39 on pages 2 and 4.

Response to Arguments

Applicant's arguments filed 1/15/08 have been fully considered but they are not persuasive.

Applicant argues that Langer fails to teach nanoparticles that are coated with nucleic acid encoding an immunogenic polypeptide and an adjuvant selected from cholera toxin, lipid A, and monophosphoryl lipid A. This is unpersuasive. As discussed above, Langer taught compositions comprising an adjuvant such as cholera toxin and cationic nanoparticles comprising a nucleic acid encoding a polypeptide antigen. See abstract and paragraphs 37, 90, 91, and 99 on pages 4, 11 and 12. Regarding Applicant's allegation that the nanoparticles are not coated with the DNA, Applicant's attention is directed to Langer at paragraphs 81 and 82 (page 10) which disclose that the nanoparticles bind the nucleic acids through charge interaction, the anionic nucleic acids adhering to the positively charged nanoparticles. Absent evidence to the contrary, this results in complexes in which the nucleic acids adhere to the surfaces of the nanoparticles. Applicant has not made clear any distinction between adherence to the surface of a nanoparticle and "coating", and has not set forth any other way in which the nanoparticle/nucleic acid complexes could form that would not result in coating of the nanoparticles, so the rejections are maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 3 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Langer et al (US 20020131951, published 3/19/02).

Langer taught compositions comprising an adjuvant such as cholera toxin and cationic nanoparticles comprising a nucleic acid encoding a polypeptide antigen. See abstract and paragraphs, 11, 37, 90, 91, and 99. The nucleic acid can be DNA or an oligonucleotide, see paragraphs 11 and 39.

Langer did not specifically teach neutral nanoparticles.

However, at paragraph 81 on page 10 Langer taught generally that the cationic polymers allowed nucleic acids to pass through membranes by reducing their charge to be neutral or slightly positive. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of the invention to use an amount of polycation that resulted in either neutral or slightly positive nanoparticles when complexed to nucleic acids.

Claims 1, 3, and 4 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Langer et al (US 20020131951, published 3/19/02) in view of Wolff et al (WO 00/03694).

Langer taught compositions comprising an adjuvant such as cholera toxin and cationic nanoparticles comprising a nucleic acid encoding a polypeptide antigen. See abstract and paragraphs, 11, 37, 90, 91, and 99. The nucleic acid can be DNA or an oligonucleotide, see paragraphs 11 and 39.

Langer did not specifically teach neutral or anionic nanoparticles.

Wolff taught that the charge of polycation/nucleic acid complexes could be adjusted by addition of polyanions, and suggested that this should be done for a variety of reasons including the fact that non-specific binding of cationic particles hinders cellular targeting (i.e. since cell membranes tend to be negatively charged, cationic particles tend to bind without specificity), and the fact that positive charge has an adverse effect on biodistribution of complexes in vivo. See page 4, lines 22-25 and page 18, lines 18-22. Wolff taught that the net charge of the recharged complexes could be positive, negative, or neutral. See page 17, lines 22-24.

It would have been obvious to one of ordinary skill in the art at the time of the invention to readjust the charge of the complexes of Langer, according to the teachings of Wolff in order to obtain the advantages disclosed by Wolff, e.g. more specific targeting, and improved biodistribution.

Claim 12 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Langer et al (US 20020131951, published 3/19/02) as applied to claims 1 and 3 above, and further in view of Deng (US 6,667,295).

Langer taught compositions comprising an adjuvant such as cholera toxin and cationic nanoparticles comprising a nucleic acid encoding a polypeptide antigen. See abstract and paragraphs, 11, 37, 90, 91, and 99. The nucleic acid can be DNA or an oligonucleotide, see paragraphs 11 and 39.

Langer did not specifically teach the use of monophosphoryl lipid A as an adjuvant.

Deng taught that either cholera toxin or monophosphoryl lipid A were suitable adjuvants for use with DNA vaccines. See column 25, lines 19-29.

MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. Furthermore, MPEP 2144.07 indicates that the selection of a known material based on its suitability for its intended use supports the determination of prima facie obviousness. Thus it would have been obvious to one of ordinary skill in the art at the time if the invention to substitute monophosphoryl lipid A for cholera toxin as an adjuvant in the invention of Langer.

Claims 1, 2, 5-7, 13, and 14 under 35 U.S.C. 103(a) as being unpatentable over Felgner et al (US 5,264,618) in view of Langer et al (US 20020131951, published 3/19/02).

Felgner taught compositions comprising complexes of nanoparticulate liposomes and nucleic acids encoding immunogens (i.e. nucleic acid vaccines), and their use to stimulate immune responses with coadministration of an adjuvant. See abstract; column 7, lines 39, 40, and 49-56; column 8, lines 5-8; column 15, lines 39-43; column 18, lines 30-33, and 43-53. The liposomes must contain cationic lipids, and can also contain neutral (e.g. phosphatidylethanolamine) and/or anionic lipids (see column 14, lines 27-33). These lipids are considered to be surfactants because they are amphiphilic. Absent a limiting definition in the instant specification, the term "oligonucleotide" is considered to embrace the antigen encoding nucleic acids of Felgner.

Felgner did not teach the use of cholera toxin as an adjuvant.

Langer taught the use of cholera toxin as an adjuvant in DNA vaccines. See abstract and paragraphs, 11, 37, 39, 90, 91, and 99.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the cholera toxin adjuvant of Langer in the invention of Felgner. MPEP 2144.07 indicates that the selection of a known material based on its suitability for its intended use supports the determination of prima facie obviousness. In this case, Felgner fails to disclose any specific adjuvant, but generally discloses that an adjuvant may be included. One of ordinary skill wishing to know what adjuvant to choose would have chosen any adjuvant suggested by the prior art for use with DNA vaccines, and the use of any of these adjuvants would have been prima facie obvious. Because Langer suggested the use of cholera toxin, the claimed invention was prima facie obvious.

Response to Arguments

Applicant's arguments filed 1/15/08 have been fully considered but they are not persuasive.

Applicant argues that Langer and Felgner fail to teach nanoparticles that are coated with nucleic acid encoding an immunogenic polypeptide and an adjuvant selected from cholera toxin, lipid A, and monophosphoryl lipid A. This is unpersuasive. As discussed above, Langer taught compositions comprising an adjuvant such as cholera toxin and cationic nanoparticles comprising a nucleic acid encoding a polypeptide antigen. See abstract and paragraphs 37, 90, 91, and 99 on pages 4, 11 and 12. Felgner taught cationic liposomal nanoparticles complexed with nucleic acids encoding antigens. Regarding Applicant's allegation that the nanoparticles are not

coated with the DNA, Applicant's attention is directed to Langer at paragraphs 81 and 82 (page 10), and Felgner at the paragraph bridging columns 2 and 3, and column 30, lines 25-41) which disclose that the nanoparticles bind the nucleic acids through charge interaction, the anionic nucleic acids adhering to the positively charged nanoparticles. Absent evidence to the contrary, this results in complexes in which the nucleic acids adhere to the surfaces of the nanoparticles. Applicant has not made clear any distinction between adherence to the surface of a nanoparticle and "coating", and has not set forth any other way in which the nanoparticle/nucleic acid complexes could form that would not result in coating of the nanoparticles, so the rejections are maintained.

Applicant also argues at pages 8 and 10 that the claimed compositions provide unexpectedly better results, relying on the specification at page 13, line 15- to page 14, line 4 and Fig. 1. This passage shows that the use of cholera toxin as an adjuvant improved the immune response to nanoparticles carrying a DNA vaccine, relative to that obtained in the absence of adjuvant. Applicant's arguments are unpersuasive because no evidence was presented that one of skill would not expect to obtain an improved immune response when using an adjuvant. Why would one use an adjuvant if not to improve the immune response? Note that even if Applicant's argument was persuasive, it would only be persuasive to the extent that the claims were limited to the conditions under which the unexpected result was obtained, i.e. with cholera toxin as an adjuvant, and with the specific nanoparticles and expression vector used in the experiment.

For these reasons the rejections are maintained.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central

fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Richard Schnizer, Ph. D./
Primary Examiner, Art Unit 1635